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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/718,996	11/21/2003	Ning Wei	KCX-742 (19795)	9086

22827 7590 07/08/2009

DORITY & MANNING, P.A.
POST OFFICE BOX 1449
GREENVILLE, SC 29602-1449

EXAMINER	
DIRAMIO, JACQUELINE A	

ART UNIT	PAPER NUMBER
1641	

MAIL DATE	DELIVERY MODE
07/08/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/718,996	WEI, NING	
	Examiner	Art Unit	
	JACQUELINE DIRAMIO	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,5,6,12 and 37-47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,5,6,12 and 37-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 October 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 27, 2009 has been entered.

Status of the Claims

2. Applicant's amendments to claims 37 and 41 are acknowledged.

3. Currently, claims 2, 5, 6, 12, and 37 – 47 are pending and under examination.

Withdrawn Objections

4. The previous objection to claim 37 is withdrawn in view of Applicant's amendment filed May 27, 2009.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claims 2, 5, 6, 12, 37 – 41, 43 and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brooks et al. (US 6,509,196), as evidenced by incorporated Brooks et al. reference (US 5,743,517), in view of Buck (US 6,258,548).

Brooks et al. teach a method for detecting an analyte in a test sample, said method comprising:

i) providing an assay device that comprises:

an application point (sample pad);

a contact region (conjugate pad) that contains test particles (detection probes) and internal control particles (calibration probes), the test particles being conjugated with a binding agent (first binding member) configured to specifically bind with the analyte;

a porous membrane in fluid communication with the application point and the contact region, the porous membrane defining a detection zone in which is immobilized a detection reagent (second capture reagent) configured for specifically binding with the analyte and a control reaction zone (calibration zone) within which is immobilized a control detection reagent (third capture reagent) configured to bind with the internal control particles, wherein the

detection zone and the control reaction zone are located downstream from the application point and contact region;

ii) contacting the assay device with the test sample, wherein a quantity of the analyte in the test sample binds to the binding agent of the test particles to form complexes that flow through the porous membrane and bind to the detection reagent in the detection zone to generate a detection signal, and wherein the internal control particles flow through the porous membrane and bind to the control detection reagent at the control reaction zone to generate a control (calibration) signal;

iii) detecting the intensity of the detection signal and the control signal; and

iv) comparing the intensity of the detection signal to the intensity of the control signal, wherein the quantity of the analyte within the test sample is proportional to the intensity of the detection signal calibrated by the intensity of the control signal (see column 1, lines 28-67; column 2, lines 1-30; column 3, lines 43-63; column 4, lines 16-50; column 5, lines 1-67; column 6, lines 1-67; column 7, lines 1-67; column 8, lines 1-31; column 9, lines 43-67; and column 10, lines 1-10).

With respect to the elements of the application point and contact region, these elements do in fact represent an application (sampling) pad and contact (conjugate) pad, wherein the contact pad includes the conjugated particles utilized in the assay device (see Figure 1; and column 4, lines 1-67 of incorporated reference of Brooks et al. (US 5,753,517), wherein this reference is incorporated in the primary reference of Brooks et al. at column 4, lines 42-50).

However, the primary reference of Brooks et al. fails to teach the inclusion of a scavenging zone within the application point, wherein the scavenging zone contains a non-

diffusively immobilized capture reagent configured to specifically bind with the analyte, and wherein a quantity of the analyte in the test sample less than or equal to a predefined base quantity binds to said capture reagent at the scavenging zone prior to the contacting of the test sample with the detection probes or detection zone.

Buck teaches a lateral flow test strip and method for detecting an analyte in a test sample utilizing the test strip, wherein the method comprises:

i) providing the lateral flow test strip (flow-through assay device) that comprises:

a wicking (sampling) pad 14 that defines an analyte modulating zone (AMZ) (scavenging zone) in which is non-diffusively immobilized a binding ligand (first capture reagent) configured to specifically bind with the analyte;

a conjugate zone or pad 18 that contains an indicator reagent (detection probes) conjugated with a specific binding ligand (member) configured to specifically bind with the analyte;

a porous membrane 12 in fluid communication with the wicking pad and the conjugate zone, the porous membrane defining an analyte test zone (ATZ) (detection zone) in which is immobilized a binding ligand (capture reagent) for the analyte, wherein the ATZ is located downstream from the wicking pad and the conjugate zone; and

ii) contacting the test strip with the test sample, wherein a quantity of the analyte in the test sample equal to a predefined base quantity binds to said immobilized binding ligand at said AMZ and a quantity of the analyte in excess of the predefined base quantity binds to the specific binding ligand of the indicator reagents to form complexes that flow through the porous membrane and bind to the immobilized binding ligand in the ATZ to generate a test (detection)

signal. The analyte modulating zone (AMZ) is included with the test strip in order to remove a fraction of the analyte from the sample prior to the sample reaching the analyte test zone (ATZ) to thereby increase the detectable range of analyte concentration, which is beneficial for samples that contain a high concentration of analyte (see Figure 1; column 2, lines 35-60; column 3, lines 30-67; column 4, lines 1-67; column 5, lines 17-34; Example 1 and Table 1).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include with the method of Brooks et al. a scavenging zone or analyte modulating zone (AMZ), wherein the sample is contacted with the AMZ prior to reaching the detection or test zone, as taught by Buck because Buck teaches the benefit of including an analyte modulating zone (AMZ) within a test strip in order to remove a fraction of an analyte from a test sample prior to the sample reaching an analyte test zone to thereby increase the detectable range of analyte concentration, which is beneficial for samples that contain a high concentration of analyte.

With respect to Applicant's claims 2 and 6, Buck teaches that the immobilized binding ligand at both said AMZ and said ATZ comprises a capture antibody (see column 2, lines 35-52; column 4, lines 36-38; column 5, lines 17-34; and Example 1).

With respect to Applicant's claims 5 and 39, Brooks et al. teach that the analyte can comprise an antigen and the detection reagent in the detection zone can comprise an antibody, antigen, or hapten (see column 4, lines 16-41; column 6, lines 41-46; and column 7, lines 8-16).

With respect to Applicant's claim 12, Brooks et al. teach that the test particles comprise a substance, such as liposomes, luminescent labels, fluorescent labels, phosphorescent particles, or latex particles (direct visual labels) (see column 5, lines 15-40).

With respect to Applicant's claim 38, both Brooks et al. and Buck teach that the contact region/conjugate pad is located downstream of the application point/wicking pad (see Brooks et al.: column 4, lines 42-50; and Buck: Figure 1).

With respect to Applicant's claim 40, Brooks et al. teach that the binding agent of the test particles can comprise an antibody (see column 5, lines 15-47).

With respect to Applicant's claim 41, Brooks et al. teach that the analyte binding agent(s) utilized within the device can comprise antibodies directed against the same or a different epitope of the analyte (see column 6, lines 39-47). Buck et al. teach that the capture molecule within both the ATZ (detection zone) and the AMZ (scavenging zone) can comprise an antibody, specifically one which binds to the analyte (see column 5, lines 18-34). Although, Example I within Buck et al. teaches that the capture molecule (i.e. antibody) within the ATZ binds to a different epitope of the analyte than the capture molecule (i.e. antibody) within the AMZ, the capture molecules or antibodies are not limited to only this embodiment (see claims 1 and 7, in particular).

Therefore, when considering the teachings of Brooks et al. in view of Buck et al., wherein Brooks et al. allow for the analyte binding agents utilized within the device to comprise antibodies directed against the same epitope of the analyte and Buck et al. merely require the capture molecules in both the ATZ and AMZ to comprise agents, such as antibodies, which both bind to the analyte, it would have been obvious to one of ordinary skill in the art at the time of

the invention to utilize antibodies that bind the same epitope of the analyte in both zones given that this is a matter of design choice and optimization absent evidence of unexpected results.

With respect to Applicant's claim 43, Brooks et al. teach that the test sample can be blood or derived from blood (see column 4, lines 24-33).

With respect to Applicant's claim 47, both Brooks et al. and Buck et al. teach the inclusion of a wicking/absorption pad within the assay device that is in fluid communication with the porous membrane and located downstream from the detection zone and the control reaction zone (see Figure 1 and column 4, lines 1-67 of incorporated reference of Brooks et al. (US 5,753,517), wherein this reference is incorporated in the primary reference of Brooks et al. at column 4, lines 42-50; and Buck: Figure 1; and column 4, lines 30-43).

6. Claims 42, 44, and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brooks et al. (US 6,509,196) in view of Buck (US 6,258,548), as applied to claim 37 above, and further in view of Selmer et al. (US 5,387,503).

The Brooks et al. and Buck references, which were discussed in the 103(a) rejection above, fail to teach that the analyte specifically comprises C-reactive protein.

Selmer et al. teach an assay method and test kit using internal calibration to measure an analyte in a test sample. The test kit comprises a solid support comprising a porous membrane defining a first and second discrete area, wherein the first discrete area contains an immobilized reagent capable of binding the target analyte and the second discrete area contains an immobilized reagent capable of binding a calibrator analyte. The test kit is suitable for detecting analytes that are of biological origin and would be carried out in doctor's office tests, wherein

one of the test analytes suitable for quantitative detection includes C-reactive protein (see column 2, lines 27-57; column 3, lines 16-25 and lines 49-55; column 4, lines 3-7 and lines 19-36; column 5, lines 4-48; column 6, lines 1-4 and lines 24-44).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include with the method of Brooks et al. and Buck the detection of C-reactive protein as taught by Selmer et al. because Selmer et al. teach that C-reactive protein represents a suitable test analyte for quantitative detection in a test assay of this type, and is also a common analyte that is detected in doctor's office tests.

With respect to Applicant's claim 45, Buck teaches that the pre-defined base quantity that represents the amount of analyte in the test sample that is removed by binding in the AMZ is empirically established during manufacturing and quality control procedures for the specific analyte, wherein the amount of analyte bound by the AMZ allows for detecting an extended range of analyte concentration (see column 5, lines 17-34; Example 1 and Table 1). Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to determine an optimum pre-defined base quantity of analyte that is bound to and removed by the AMZ as taught by Buck in order to optimize the assay method and allow for the detection of an extended range of analyte concentration.

7. Claim 46 is rejected under 35 U.S.C. 103(a) as being unpatentable over Brooks et al. (US 6,509,196) in view of Buck (US 6,258,548), as applied to claim 37 above, and further in view of Jou et al. (US 5,670,381).

The Brooks et al. and Buck references further fail to teach that the control detection reagent in the control reaction zone comprises a polyelectrolyte having a net charge opposite to the net charge of the test particles and/or internal control particles.

Jou et al. teach a device for performing an assay comprising a porous material containing a capture or reaction zone with an immobilized capture reagent. The device utilizes a specific binding member attached to a charged substance that is contacted with an analyte of interest to form a complex. The complex binds to the immobilized capture reagent in the capture or reaction zone through ion-capture, wherein the capture reagent is oppositely charged with respect to the charged substance of the analyte complex. The capture reagent preferably comprises an anionic or cationic polymeric substance (polyelectrolyte), which enables the production of a generic solid phase device for use in specific binding assays. Assay procedures for many different analytes can use the same solid phase material which contains a predetermined zone of anionic or cationic capture polymer rather than an immobilized binding member capable of binding only a specific analyte as found in conventional flow-through or test- strip devices. Further, the ion-capture technique increases the potential number of complexes that can be immobilized on the solid support (see column 6, lines 25-40; column 7, lines 1-46; column 10, lines 63-65; column 19, lines 29-67; column 22, lines 29-67; and column 23, lines 1-26).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include with the method of Brooks et al. and Buck a polyelectrolyte as the reagent in the control reaction zone as taught by Jou et al. because Jou et al. teach the benefit of using an anionic or cationic polymeric substance as the immobilized capture reagent in a capture zone because the polymeric substance allows for the binding of a conjugated substance or

complex to a solid phase support material through ion-capture, which increases the potential number of complexes that can be immobilized on the solid support and allows for the production of a generic solid phase device, wherein many different analytes can use the same solid phase material which contains a predetermined zone of anionic or cationic capture polymer rather than an immobilized binding member capable of binding only a specific analyte as found in conventional flow-through or test-strip devices. In addition, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the labeled reagent in the conjugate zone and the capture reagent in the control zone of Brooks et al. with the charged labeled reagent and the polyelectrolyte taught by Jou because this change is a mere alternative and functionally equivalent labeling and capturing technique. One having ordinary skill in the art would have been motivated to make such a change since only the expected labeling effect would have been obtained, and changes such as these are routinely made based on the economics and availability of components.

Response to Arguments

8. Applicant's arguments filed May 27, 2009 have been fully considered but they are not persuasive. Applicant main argument (see pages 7-8) is that it would not have been obvious to combine Buck et al. with Brooks et al. because one of ordinary skill in the art would not have reasonably looked to Buck et al. to solve the problem of excess analyte when that was not even a problem in Brooks et al.

However, this argument is not found persuasive.

With respect to Applicant's argument, when determining obviousness, neither the particular motivation to make the claimed invention nor the problem the inventor is solving controls. The proper analysis is whether the claimed invention would have been obvious to one of ordinary skill in the art after consideration of all the facts (see MPEP § 2141). Thus, Applicant's argument that because Brooks et al. were not concerned with the problem of excess analyte, one of ordinary skill in the art would not have looked to Buck et al. to solve this problem, is considered irrelevant. The references together must be considered in their entirety, for both their teachings and motivation, and the fact that Brooks et al. is not concerned with the problem of excess analyte is NOT a controlling factor. The Buck et al. reference was cited for its disclosure of and motivation for including an AMZ, i.e. analyte modulating zone (scavenging zone), within a test device, wherein Buck teaches the benefit of including an analyte modulating zone (AMZ) within a test strip in order to remove a fraction of analyte from a test sample prior to the sample reaching an analyte test zone to thereby increase the detectable range of analyte concentration, which is beneficial for samples that contain a high concentration of analyte. Therefore, given this teaching of and motivation for including an analyte modulating zone (i.e. scavenging zone) within a test strip device and method of use as taught by Buck, it would have been obvious to include this zone with the method and device of Brooks et al., which comprise comparable elements and operation to the methods and devices of Buck, in order to achieve these benefits taught by Buck.

In addition, Applicant argues (see pages 8-9) that the prior art references fail to teach the limitations recited in Applicant's amended claim 41. However, this argument is not found persuasive for the reasons discussed in the 103(a) rejection above. Brooks et al. teach that the

analyte binding agent(s) utilized within the device can comprise antibodies directed against the same or a different epitope of the analyte (see column 6, lines 39-47). Buck et al. teach that the capture molecule within both the ATZ (detection zone) and the AMZ (scavenging zone) can comprise an antibody, specifically one which binds to the analyte (see column 5, lines 18-34). Although, Example I within Buck et al. teaches that the capture molecule (i.e. antibody) within the ATZ binds to a different epitope of the analyte than the capture molecule (i.e. antibody) within the AMZ, the capture molecules or antibodies are not limited to only this embodiment (see claims 1 and 7, in particular).

Therefore, when considering the teachings of Brooks et al. in view of Buck et al., wherein Brooks et al. allow for the analyte binding agents utilized within the device to comprise antibodies directed against the same epitope of the analyte and Buck et al. merely require the capture molecules in both the ATZ and AMZ to comprise agents, such as antibodies, which both bind to the analyte, it would have been obvious to one of ordinary skill in the art at the time of the invention to utilize antibodies that bind the same epitope of the analyte in both zones given that this is a matter of design choice and optimization absent evidence of unexpected results.

Conclusion

9. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JACQUELINE DIRAMIO whose telephone number is (571)272-8785. The examiner can normally be reached on M-F 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on 571-272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jacqueline DiRamio/
Examiner, Art Unit 1641

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